

# Childhood Cancer Canada Funding

## Message from the Executive Director

For 25 years Childhood Cancer Canada Foundation, formerly under the banner Candlelighters, has been the steady and significant supporter of children with cancer in Canada. After partnering in 2003 with the C<sup>17</sup> Council, both organizations have developed and risen to the challenge of addressing the pressing needs of children with cancer. Whether through research grants, education, making sure children can access experimental drugs and international research trials, setting national guidelines or advocating on a national level, the partnership has promoted some huge success stories. Over 30 research grants have been funded and over 200 clinical trials have opened in Canada; 17 centres across Canada are linked to national education and evidence-based clinical guidelines to provide Canadian children access to the best treatment and the best quality of cure and quality of life we can develop.

Our partners are growing, our capacity in Canada to conduct research is growing, and last year we handed out just under \$1 million in our research and education grants program. A huge leap from the \$23,750 we handed out in 2005. Last year we were recognized in the CCRA publication *Cancer Research Investment in Canada, 2005-2009* for an incredible 1869% increase in the grant funding we have disbursed.

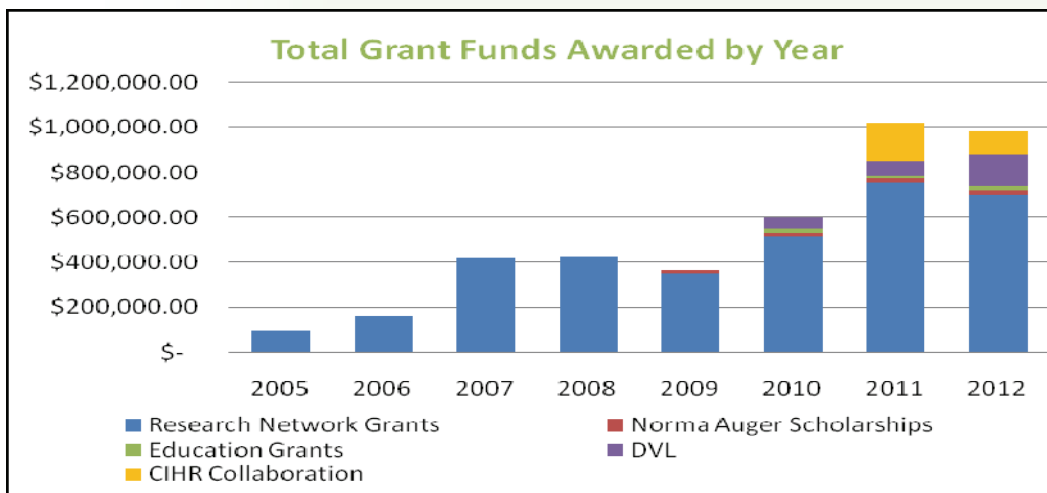
An important aspect of the funding we receive and distribute is what happens after the money is sent and spent. What happens to the results, what do the researchers do next? In this report, we highlight some of the publications and knowledge translation activities and “next steps” that have been undertaken by our funded researchers. They are publishing and presenting their work, and taking the time to teach it to others. Some, such as Dr. Klassen and Dr. Dror, are on their second or third grant from C<sup>17</sup>. Some have gathered and analyzed tumours, tissue and treatment information, and are now trying to develop better treatments. Others, such as Dr. Mabbott and Dr. Rassekh are members of larger CIHR Teams that were awarded over \$12.5 million to study and treat or prevent late effects in childhood cancer survivors.



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*C<sup>17</sup> strives to improve health outcomes and quality of life for children and adolescents in Canada with cancer and blood disorders, and to eliminate disparities in care and outcomes wherever they occur*



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## Prospective Cohort Study of Genetic Variation and Risk of Infection in Canadian Children with Acute Myeloid Leukemia

Dr. Lillian Sung, Hospital For Sick Children

\$17,000 funded in 2005

Final Report: August 2011.

This research was a prospective cohort study with the primary objective of determining the relationship between single nucleotide polymorphisms in genes of immunity and the risk of invasive infection in children with acute myeloid leukemia (AML). In June 2008, Sung and her team were in their third year of patient recruitment. The study was open and accruing patients at 17 centres (15 Canadian and 2 American) and they had enrolled 102/300 subjects. Adequate DNA from all children had been obtained to complete the proposed candidate gene studies.

They received a 3 year operating grant in 2005 from NCIC; successfully renewing the grant for 4 years beginning in July 2008. The C<sup>17</sup> funding was provided to the team to encourage them to open the study at all Canadian C<sup>17</sup> centres interested in participating.

The results of this study were presented at the Sick Kids Research Institute, in 2008 and 2009: *Predicting the Risk of Infection in Children Receiving Chemotherapy for Acute Myeloid Leukemia*. While the most common causes of invasive fungal infections (IFI) in pediatric AML are caused by *Candida* and *Aspergillus*, this research has highlighted the importance of being aware of the possibility of other causes of IFI in these children. Their comprehensive publication in 2010 describes several incidences of *Alternaria* sinusitis in children with acute myeloid leukemia (Maloney et al, Leuk Lymphoma, 2010).

## Genotype-Specific Approaches to Therapy in Children with Cancer (GATC Cancer).

Dr. Rod Rassekh, BC Children's Hospital

\$114,800 funded in 2006

Final Report: February 2012

This research, with the support of C<sup>17</sup>, was able to partner with the larger pediatric genome study (GATC) and include a focus on identifying genetic factors in pediatric cancers. The cisplatin study initially identified two genes associated with cisplatin induced hearing loss (Ross et al, Nature Genetics, 2009). Cisplatin is a frequently used chemotherapy drug used for the treatment of solid tumours. Further work has identified a third gene that appears to be associated with hearing loss due to cisplatin (Pussegoda et al, submitted). A prediction model using clinical and genetic factors has been created in order to help clinicians place subjects into risk groups to try and keep high survival outcomes and reduce the risk of hearing loss.

The anthracycline study has identified a gene that appears to be associated with anthracycline cardiac toxicity. Anthracyclines are used to treat a wide variety of solid tumours, and a well known long term effect is damage to the heart. The gene is a drug transporter that enables medications to enter cells. A low functioning variant in this gene could result in less anthracycline entering the cardiac myocyte and therefore less toxicity to these cells. In addition a genetic/clinical prediction was created that classifies subjects into low, intermediate and high risk of cardiac toxicity. Identifying patients with potential for later heart failure means that surveillance and treatment can start earlier to try and avoid serious outcomes. This work was published recently in the Journal of Clinical Oncology (Visscher et al, JCO, 2011).

The researchers have developed numerous follow-up studies including a successful CIHR competition that partnered with numerous funding groups, including C<sup>17</sup> on a 5 year team grant that will look to mitigate cisplatin hearing loss through the use of an otoprotectant drug for those identified as high risk of toxicity. In addition whole genome studies will be performed in both the anthracycline and cisplatin groups to identify other genes of interest. They are also expanding to investigate renal (kidney) outcomes in those who received cisplatin. Other genetic results are now being investigated in a Children's Oncology Group study as part of a sodium thiosulfate otoprotectant trial.



## Osteonecrosis in Children with Acute Lymphoblastic Leukemia

Dr. Jacqueline Halton, CHEO

**\$133,591 funded in 2008** Study to be completed January 2013

Acute Lymphoblastic Leukemia is the most common form of childhood cancer with current treatment survival rates approaching 80%. Improved outcomes show an increased number of survivors at risk for long-term treatment related side effects including osteonecrosis. Osteonecrosis, or bone death, is caused by blood supply loss to the bone causing pain and poor quality of life. The hips, shoulders, knees and ankles may be affected. Pain is the usual presenting symptom and may become severe requiring surgical decompression or replacement of the affected joint. Long term effects including arthritis and progressive joint difficulties may not be known for decades. This study is trying to determine risk factors for developing osteonecrosis through MRIs of patients treated for leukemia that will lead to information for earlier detection and prevention. The study will be the basis for future intervention and prevention trials. Currently ten C<sup>17</sup> sites participating have ethics approval, and 51 of 162 potential patients have consented. All sites should have the remaining eligible patients enrolled by December 2012. 38 MRIs have been scored to date and the remainder are being scheduled.

## Characterization of myelodysplastic syndrome secondary to inherited marrow failure syndromes and the spectrum of inherited marrow failure syndromes through the Canadian Inherited Marrow Failure Registry (CIMFR)

Dr. Yigal Dror, Hospital For Sick Children

**\$120,300 funded in 2009** Final Report: August 2012.

The first aim of this study was *“To characterize the spectrum of novel and previously categorized syndromes with inherited bone marrow failure.”* Dror and his team were able to analyze the clinical and genetic data of 76 patients with inherited bone marrow failure syndromes (IBMFSs). They studied both those with an identified genetic background and an additional 183 patients without known genotype (enrolled on the Canadian Inherited Marrow Failure Registry (CIMFR)). They found that disease-causing mutations could be identified in 53.5% of the 142 patients tested, and in 16 different genes. Ten novel mutations were identified. Their complete findings for this study were published (Tsangaris E, et al., J Medical Genetics 2011 48:618-28). The second project focused on one relatively common IBMFS. They found that the diagnosis of Shwachman-Diamond syndrome (SDS), Diamond Blackfan anemia, Fanconi anemia (FA) were often delayed relative to symptoms onset; indicating a major need for improving tools to establish a rapid diagnosis. These results were also published (Hashmi S et al., Clinical Genetics, 2011; 79(5):448-58).

The second aim was *“Determining the outcome and unique features of IBMFS-related MDS.”* Many of the IBMFSs are leukemia predisposition syndromes. They found that among 327 IBMFS patients enrolled on the CIMFR, 45 (13.8%) developed clear evidence of clonal and malignant myeloid transformation. These IBMFS were further classified and followed. This data was submitted for presentation to the EWOG Bone Marrow Failure and MDS conference in November 2012 and for the American Society of Hematology Meeting in December 2012.

### OVERVIEW: ALL FUNDED GRANTS

2005

#### Prospective Cohort Study of Genetic Variation and Risk of Infection in Canadian Children with Acute Myeloid Leukemia

Dr. Lillian Sung, Hospital for Sick Children

#### Defining the Clinical Phenotype of Inherited Marrow Failure Syndromes and the Risk Factors for Severe Hematological Complications and Cancer by the Canadian Inherited Marrow Failure Registry (CIMFR)

Dr. Yigal Dror, Hospital for Sick Children

2006

#### The effect of maintaining a higher hemoglobin level on neutropenia duration after bone marrow transplantation in children: a pan-Canadian multicenter randomized controlled clinical trial

Dr. Michel Duval, Hopital Ste. Justine

#### Genotype-Specific Approaches to Therapy in Children with Cancer (GATC Cancer)

Dr. Rod Rassekh, BC Children's Hospital

2007

#### Neuro-imaging of White Matter and Neuro-cognitive Outcomes following Cranial Radiation for Pediatric Brain Tumours

Dr. Donald Mabbott, Hospital for Sick Children

#### Immigrant Families' Experiences of Care for their Child with Cancer

Dr. Anne Klassen, McMaster

#### Evaluation of Biomarkers in Relation to Recurrence Rate in Childhood Ependymoma

Dr. Juliette Hukin, BC Children's Hospital

#### The Role of Intrathecal Methotrexate, Triple Intrathecal Therapy, and High Dose Intravenous Methotrexate in Predicting Neurocognitive Outcome in Survivors of Childhood Leukemia

Dr. Andrea Downie, Children's Hospital (London)

2008

#### Osteonecrosis In Children With Acute Lymphoblastic Leukemia

Dr. Jacqueline Halton, Children's Hospital of Eastern Ontario (CHEO)

## 2008 Continued

**ADP Signaling Defect as a Potential Cause for Aplastic Anemia**

Dr. Evan Shereck (new PI Dr. Kirk Schultz)  
BC Children's Hospital

**Relationship of Prothrombotic Markers to Thrombosis in Survivors of Childhood Cancer**

Lesley Mitchell, University of Alberta

**Sandra Sharpe Rhabdomyosarcoma Fund  
The Estrogen Receptor Pathway as a Therapeutic Target in Rhabdomyosarcoma**

Dr. David Malkin, Hospital for Sick Children

## 2009

**Development of the P-SCS: The Pediatric Supportive Care Scale**

Dr. Shayna Zelcer, Children's Hospital (London)

**Thalamic Brain Tumours in Canada in the MRI Era**

Dr. Paul Steinbok, BC Children's Hospital

**Characterization of Myelodysplastic Syndrome Secondary to Inherited Marrow Failure Registry (CIMFR)**

Dr. Yigal Dror, Hospital for Sick Children

## 2010

**A Randomized Controlled Multicenter Non-Inferiority Trial of Twice Daily Low Dose Dexamethasone versus High Dose Dexamethasone for Symptom Control in Children with a Brain Tumour Undergoing Cranial or Craniospinal Radiation**

Dr. Ute Bartels, Hospital for Sick Children

**Central venous line dysfunction as a predictor of thromboembolism in children with cancer**

Dr. Uma Athale, McMaster University

**The Relationship between Cyclosporine Area under the Curve and Acute Graft Versus Host Disease in Children undergoing Haematopoietic Stem Cell Transplant**

Dr. Lee Dupuis, Hospital for Sick Children

**Central Venous Line Dysfunction as a Predictor of Thromboembolism in Children with Cancer**

**Dr. Uma Athale**

**\$198,400 funded in 2012 Study to be completed in August 2013**

This is a multi-institutional observational study which is open for patient enrollment in five participating institutions: Children's Hospital of Eastern Ontario, Children's Hospital (London Health Sciences Center), Kingston General Hospital, The Hospital for Sick Children, and McMaster Children's Hospital. There has been very good progress in logistics, ethics approval and patient enrollment. Progress has been made in the development of the database. With consensus of all five investigators, data collection forms were developed. Once the forms were finalized, the forms were then converted into "Teleform" acceptable format ready to use.

Athale and her team have evaluated the effects of body mass index (BMI) on the risk of thromboembolism in children with hematological malignancies. These findings have been presented at the International Society on Thrombosis and Haemostasis (ISTH), in Kyoto, Japan (2011). They have also resulted in a publication (Tuckuviene, R., Pediatric Blood Cancer. 2012 Aug; 59(2):320-2). A second publication specific to central venous line dysfunction is in preparation (2012).

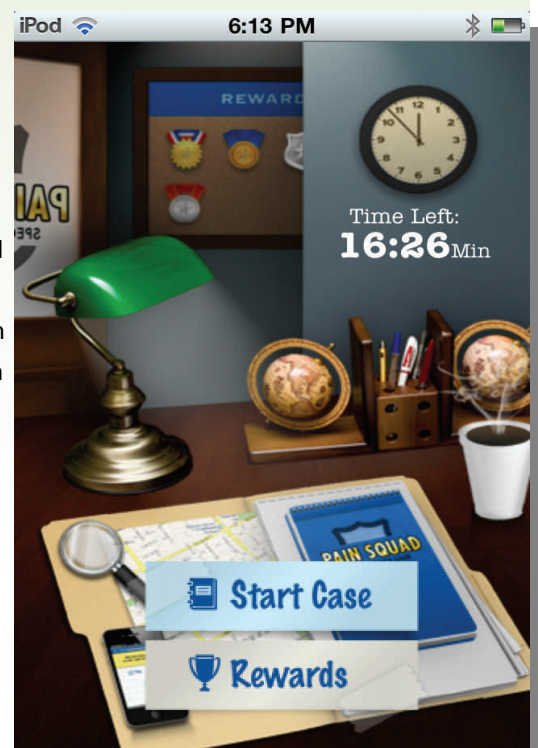
**Development and Testing of a Multidimensional Electronic Pain Diary for Youths with Cancer**

**Dr. Jennifer Stinson**

**\$199,929 funded in 2011 Study to be completed January 2013**

Original plans to modify the existing eOuch pain diary, were not feasible due to the outdated technological nature of the eOuch pain diary. A competitive procurement process was initiated in order to identify an iPhone application developer to modify and create the cancer pain diary. The selected vendor was Cundari Group Ltd. And over a 5-month period, the "Pain Squad" iPhone application was developed via an in-kind donation of services. The application consists of a 24-item cancer pain survey, evaluating the sensory, affective, and evaluative dimensions of pain using interactive features such as sliding 5cm visual analog scales, body maps, video clips and open text fields.

The "Pain Squad" application is based on a police detective theme which is embedded throughout the application along with an internal rewards system (e.g., achieving higher rankings – rookie to chief of police) to enhance compliance. Included video clips have also been designed to enhance compliance through messages of support from actors of CTV's police drama "Flashpoint" and Global TV's "Rookie Blue".



## What Factors Do Children With Cancer And Childhood Cancer Survivors Say Are Important To Understanding Their Quality Of Life? A Qualitative Study

**Principal Investigator: Dr. Anne Klassen, McMaster University**

**\$156,093 funded in 2011 Study to be completed August 2014**

Research Ethics Board and grant agreements are now in place for all 4 centres: McMaster University, Children's Hospital of Eastern Ontario, Sick Kids and BC Children's Hospital. Data collection has commenced and a total of 20 interviews with pediatric cancer patients and survivors have been conducted at McMaster and CHEO. The interviews have been transcribed verbatim and data analysis is presently underway, with data managed within computer software (N'Vivo). Knowledge translation and dissemination efforts include: S.H.A.R.E. - Survivors' Health: Advocating for Resources and Education for Childhood Cancer Survivors 4th Con-



ference in Ottawa, October 2011 – Invited Speakers

International Society of Paediatric Oncology, 44th Congress, London, October 2012 – 'Factors important to understanding quality of life according to children with cancer and childhood cancer survivors' - Submitted Abstract

International Society of Quality of Life, 19th International Conference, Budapest, October 2012 – 'Refining a Conceptual Framework of HR-QOL within Pediatric Oncology' – Abstract accepted for Child Health Symposium

## Parent, provider, and survivor perspectives of investigational fertility preservation interventions for pre-pubertal boys with cancer: Exploring the factors influencing decisions and measuring preferences

**Principal Investigator: Dr. Armando Lorenzo**

**\$79,054 funded 2012**

**Results pending**

Many cancer treatments can damage a boy's reproductive organs, making him unable to have a baby later in life. For adolescents who have gone through puberty, freezing sperm is a standard way to maintain their future ability to have a baby. Unfortunately, for boys who have not gone through puberty, there are no similar options. This is because young boys cannot produce sperm to be frozen. Recent research has shown that it is possible to grow sperm from tissue that is from an immature mouse testicle to father baby mice. It is likely that similar technology will be available for humans. Dr. Lorenzo and Dr. Gupta would like to offer testicle tissue freezing to young boys with cancer so that when technology to grow sperm is available; boys will have the possibility to father their own children. However, before this is offered, these doctors will complete a study to gather information from parents, healthcare workers, and adolescent cancer survivors about desires and obstacles to starting tissue freezing. This research will help Dr. Lorenzo and Dr. Gupta develop a fertility program for boys across Canada that will provide survivors hope of fathering their own children and ultimately improve quality of life.

2011

### Development and Testing of a Multi-dimensional Electronic Pain Diary for Youths with Cancer.

Dr. Jennifer Stinson, Hospital for Sick Children

### Identification of prognostic factors and therapeutic targets in childhood CNS atypical teratoid rhabdoid tumours (ATRT).

Dr. Lucie Lafay-Cousin, Alberta Children's Hospital

### What factors do children with cancer and childhood cancer survivors say are important to understanding their quality of life? A qualitative study

Dr. Anne Klassen, McMaster University

### Assessing the efficacy of a psychosocial intervention program for siblings of children with cancer

Dr. Maru Barrera, Hospital for Sick Children

2012

### Bone Marrow failure-causing alleles in Canada and genotype phenotype correlation

Dr. Yigal Dror, Hospital for Sick Children

### Generation and Validation of the Self PBQ

Dr. Paula James, Queens University

### Parent, provider, and survivor perspectives of investigational fertility preservation interventions for pre-pubertal boys with cancer: Exploring the factors influencing decisions and measuring preferences

Dr. Armando Lorenzo, Hospital for Sick Children

### Elucidation of YB-1 as a metastatic driver through angiogenic mechanisms in Ewing family tumours using zebrafish and mouse models

Dr. Jason Berman, IWK Health Centre



## Developmental Therapeutics 2011

**Potential for PLK inhibitors in leukemia**  
Dr. Aru Narendran, AB Children's Hospital

**Potential for PLK inhibitors in CNS tumours**  
Dr. Sandi Dunn, BC Children's Hospital

**Potential for PLK inhibitor in neuroblastoma and sarcomas**  
Dr. Sylvain Baruchel, Hospital for Sick Children

**Pharmacogenetic analysis of cyclophosphamide metabolism in pediatric acute lymphoblastic leukemia patients**  
Dr. Richard Kim, Children's Hospital (London)

**In vivo anti-tumor and anti-metastatic activity and functional imaging of palifosfamide in preclinical neuroblastoma models**  
Dr. Sylvain Baruchel, Hospital for Sick Children

Childhood Cancer Canada has a partnership with the St. Baldrick's Foundation in the USA to run St. Baldrick's events in Canada. The funds raised through these head-shaving events will be used to support research in C<sup>17</sup>.

In March 2012, \$250,000 was received from Childhood Cancer Canada from the St. Baldrick's events. This year the funds were used to help support the research grant competitions, adjudicated in June 2012. In partnership with our funders, we funded the following:

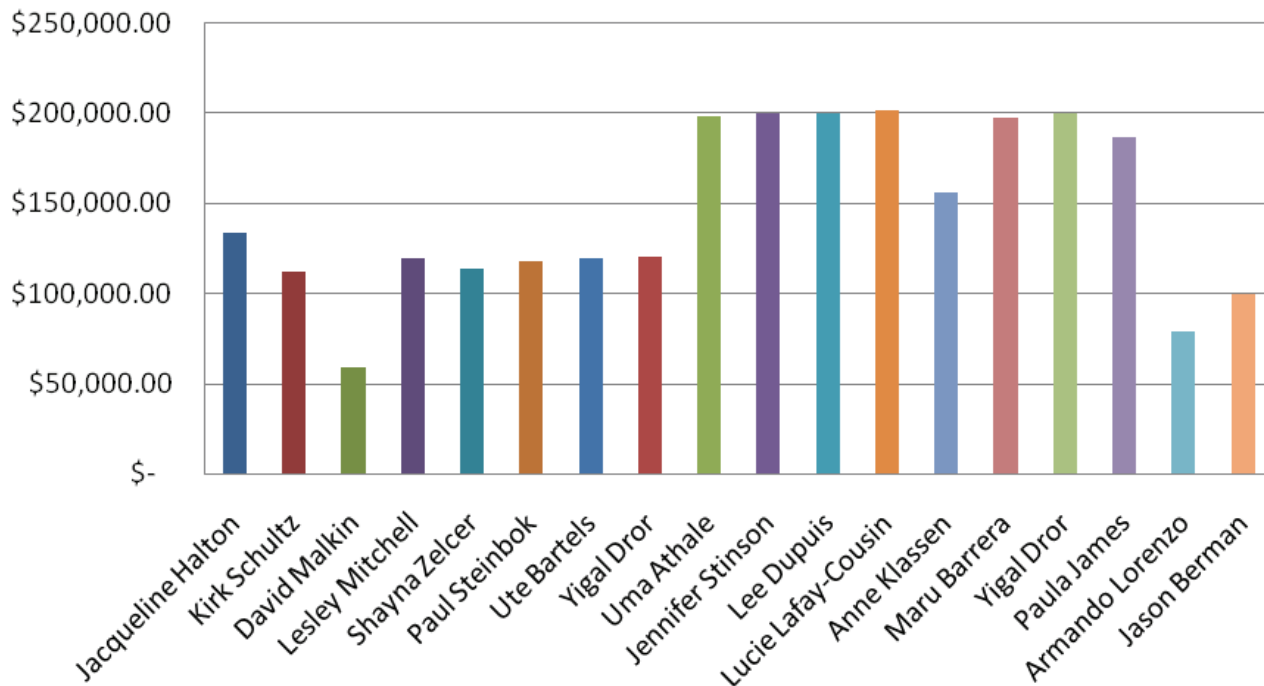
Yigal Dror, Hospital for Sick Children (2012)	\$200,000.00
Paula James, Queen's University	\$186,500.00
Armando Lorenzo, Hospital for Sick Children	\$79,054.00

Funds were also awarded in the C<sup>17</sup> Developmental Therapeutics Network grants competition. This network is linking 8 Canadian centres to conduct research in the lab that has a high probability of being able to be translated into small, early Phase I/II experimental studies in the clinics in the 8 centre.

Researchers who received funding include:

Sylvain Baruchel, Hospital for Sick Children	\$45,000.00
Richard Kim, Children's Hospital (London)	\$25,830.00

## C<sup>17</sup> Research Network Grants funded: 2008 - 2012



**Thank you for supporting pediatric oncology research in Canada. This would not be possible without the generosity of people supporting the Childhood Cancer Canada Foundation. If you are interested in any of these projects, please contact us or check for additional information on the C<sup>17</sup> website at [www.c17.ca](http://www.c17.ca)**